IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 10/516,344 Confirmation No. 9502
Applicant : Mertin et al.
Filed : November 30, 2004
Title : ORAL PHARMACEUTICAL PREPARATIONS COMPRISING ION EXCHANGE RESINS WITH ACTIVE SUBSTANCE LOADING AND PSEUDOPLASTIC GEL-FORMER THICKENERS
Group Art Unit : 1618
Examiner : Paul Dickinson

VIA EFS

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.132

Dr. Olaf Behrend, declares and states as follows:

1. I received a university diploma degree in Chemical Engineering in 1996 from Karlsruhe University. Thereafter, I received a doctoral degree in Chemical Enginnering in 2002 from Karlsruhe University.

2. From November 2007 to January 2009, I was employed by Bayer HealthCare AG and then subsequently Bayer Animal Health GmbH. My present position is formulation scientist, with Boehringer Ingelheim Pharma GmbH & Co. KG.

3. Under my direction and control, a study to compare the shear viscosity and yield strength of compositions including pradofloxacin and other excipients was conducted. Five formulations were prepared as can be seen on the attached supporting documents (Attachment 1). One

formulation included enrofloxacin and the other four formulations included pradofloxacin. The pradofloxacin formulation of the present invention is listed as formulation number 5 and included pradofloxacin trihydrate, amberlite IRP 64, sorbic acid, ascorbic acid, propylene glycole, xanthan gum, and vanilla flavour. Formulation number 1 included pradofloxacin trihydrate, amberlite IRP 64, sorbic acid, propylene glycole, lactic acid, sodium hydroxide, silica, and malt syrup 80%. Formulation number 2 included enrofloxacin, amberlite IRP 64, sorbic acid, propylene glycole, lactic acid, sodium hydroxide, silica, and malt syrup 80%. Formulation number 3 included pradofloxacin trihydrate, amberlite IRP 64, sorbic acid, propylene glycole, lactic acid, sodium hydroxide, and silica. Formulation number 4 included pradofloxacin trihydrate, amberlite IRP 64, sorbic acid, propylene glycole, lactic acid, sodium hydroxide, and a higher level of silica then formulation 3.

4. The shear viscosity and yield point were measured for all 5 formulations using a rotational viscosimeter.

5. Formulation 1 had a shear viscosity of 59 mPa*s at 150 s^{-1} and no detectable yield point. Formulation 2 had a shear viscosity of 66 mPa*s at 150 s^{-1} and no detectable yield point. Formulation 3 had a shear viscosity of 15 mPa*s at 150 s^{-1} and no detectable yield point. Formulation 4 had a shear viscosity of 80 mPa*s at 150 s^{-1} and no detectable yield point. Finally, Formulation 5 had a shear viscosity of 334 mPa*s at 150 s^{-1} and a yield point of 15.

6. As can be observed based on these results, Formulation 5 that included xanthan had a higher shear viscosity and actually had a yield point. Formulations 1-4 that did not include xanthan, but included silica, had a lower shear viscosisty and no detectable yield point. This dramatic

difference in shear viscosity and yield point is not anticipated on the basis of the minor change in the composition.

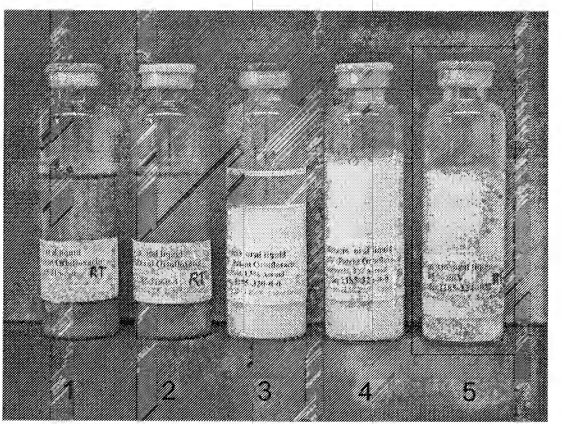
7. The signee further declares that all statements made herein are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dr. Olaf Behrend

2009-09-19

Date

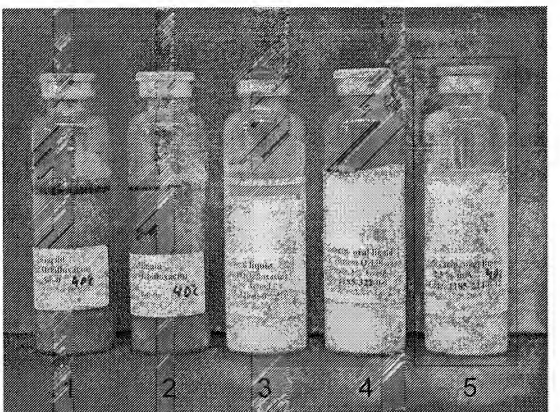
Stability screening: storage for 1 week at RT



1. **formulation according to example 2** (pradofloxacin)
2. **formulation according to example 2** (enrofloxacin)
3. formulation according to example 2, w/o malt syrup (pradofloxacin)
4. formulation according to example 2, w/o malt syrup plus additional SiO_2 (pradofloxacin)
5. **BAH fomulation** (Prado oral suspension)

Bayer HealthCare
Animal Health

Stability screening: storage for 1 week at 40 °C



1. **formulation according to example 2** (pradofloxacin)
2. **formulation according to example 2** (enrofloxacin)
3. formulation according to example 2, w/o malt syrup (pradofloxacin)
4. formulation according to example 2, w/o malt syrup plus additional SiO_2 (pradofloxacin)
5. **BAH fomulation** (Prado oral suspension)

Bayer HealthCare
Animal Health

Rheological properties

formulation no.	description	shear viscosity ($150\ s^{-1}$) [m Pa s]	yield stress [Pa]
1	formulation according to example 2 (pradofloxacin)	59	--- *)
2	formulation according to example 2 (enrofloxacin)	66	--- *)
3	formulation according to example 2, w/o malt syrup (pradofloxacin)	15	--- *)
4	formulation according to example 2, w/o malt syrup plus additional SiO_2 (pradofloxacin)	80	--- *)
5	BAH fomulation (Prado Oral Suspension)	334	15

*) non-detectable with standard measuring equipment

Bayer HealthCare
Animal Health

Composition of the tested formulations

100 mL of the suspension contain (quantities in g, demineralized water ad 100 mL):

	form. no. 1 (1185-318-0-0)	form. no. 2 (1185-319-0-0)	form. no. 3 (1185-320-0-0)	form. no. 4 (1185-322-0-0)	form. no. 5 (1185-224-0-12)
pradofloxacin trihydrate	3.0	-	3.0	3.0	2.5
enrofloxacin	-	3	-	-	-
amberlite IRP 64	15	15	15	15	10
sorbic acid	0.1	0.1	0.1	0.1	0.2
ascorbic acid	-	-	-	-	0.02
propylene glycole	10	10	10	10	30
xanthan gum	-	-	-	-	0.7
lactic acid	0.67	0.85	0.67	0.67	-
sodium hydroxide	0.65	0.75	0.65	0.65	-
silica	1.5	1.5	1.5	3.0	-
malt syrup 80%	30	30	-	-	-
vanilla flavour	-	-	-	-	0.2